

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
 United States Patent and Trademark
 Office
 Box PCT
 Washington, D.C.20231
 ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 06 October 1999 (06.10.99)	Applicant's or agent's file reference P5439WO CTH
International application No. PCT/GB99/00070	Priority date (day/month/year) 09 January 1998 (09.01.98)
International filing date (day/month/year) 08 January 1999 (08.01.99)	
Applicant WILLIAMS, Neil, Andrew et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

03 August 1999 (03.08.99)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Lazar Joseph Panakal Telephone No.: (41-22) 338.83.38
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PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

09/600060
For receiving office use only

PCT/GB 99/00070
International Application No.

08 JANUARY 1999
International Filing Date

United Kingdom Patent Office
PCT International Application
Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference
(if desired) (12 characters maximum) **P5439WO CTH**

Box No. I	TITLE OF INVENTION MEDICAMENT SUBSTANCE	
Box No. II	APPLICANT	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)		This person is also inventor.
OraTol Limited The Old Blue School Lower Square Isleworth Middlesex TW7 6RL		Telephone No. Facsimile No. Teleprinter No.
State (i.e. country) of nationality: [UK] GB	State (i.e. country) of residence: [UK] GB	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input checked="" type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box		
Box No. III	FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)		This person is:
WILLIAMS Neil Andrew 16 The Court Old Coach Road Cross, Axbridge Somerset, BS26 2EF United Kingdom		<input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor inventor only (if this check-box is marked, do not fill in below)
State (i.e. country) of nationality: [UK] GB	State (i.e. country) of residence: [UK] GB	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box		
<input checked="" type="checkbox"/> Further applicant and/or (further) inventors are indicated on a continuation sheet		
Box No. IV	AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE	
The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:		<input checked="" type="checkbox"/> agent <input type="checkbox"/> common representative
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)		Telephone No.
HARDING, Charles Thomas D Young & Co 21 New Fetter Lane London EC4A 1DA United Kingdom		+44 1703 634816
		Facsimile No.
		+44 1703 224262
		Teleprinter No.
		477667 YOUNGS G
Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.		

Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS

If none of the following sub-boxes is used, this sheet is not to be included in the request.

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

X
HIRST, ~~Professor~~ Timothy Raymond
30 Albert Road
Clevedon
North Somerset
BS21 7RR
United Kingdom

This person is:

- ☐ applicant only
☒ applicant and inventor
☐ inventor only (if this check-box is marked, do not fill in below)

State (i.e. country) of nationality:

~~UK~~ GB

State (i.e. country) of residence:

~~UK~~ GB

This person is applicant for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

BIENENSTOCK, John
436 Wellington Street West
Toronto
Ontario
Canada
M5V 1E3

This person is:

- ☐ applicant only
☒ applicant and inventor
☐ inventor only (if this check-box is marked, do not fill in below)

State (i.e. country) of nationality:

UK ~~and CA~~

State (i.e. country) of residence:

CA

This person is applicant for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only
☐ applicant and inventor
☐ inventor only (if this check-box is marked, do not fill in below)

State (i.e. country) of nationality:

State (i.e. country) of residence:

This person is applicant for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only
☐ applicant and inventor
☐ inventor only (if this check-box is marked, do not fill in below)

State (i.e. country) of nationality:

State (i.e. country) of residence:

This person is applicant for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Further applicants and/or (further) inventors are indicated on a continuation sheet

Box No. V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

Regional Patent

- ☒ **AP** **ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ **EA** **Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ **EP** **European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ **OA** **OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if any other kind of protection or treatment desired, please specify on dotted line)

National Patent (if other kind of protection or treatment desired, specify on dotted line):

- | | |
|--|--|
| <input checked="" type="checkbox"/> AL Albania | <input checked="" type="checkbox"/> LT Lithuania |
| <input checked="" type="checkbox"/> AM Armenia | <input checked="" type="checkbox"/> LU Luxembourg |
| <input checked="" type="checkbox"/> AT Austria | <input checked="" type="checkbox"/> LV Latvia |
| <input checked="" type="checkbox"/> AU Australia | <input checked="" type="checkbox"/> MD Republic of Moldova |
| <input checked="" type="checkbox"/> AZ Azerbaijan | <input checked="" type="checkbox"/> MG Madagascar |
| <input checked="" type="checkbox"/> BA Bosnia and Herzegovina | <input checked="" type="checkbox"/> MK The former Yugoslav Republic of Macedonia |
| <input checked="" type="checkbox"/> BB Barbados | |
| <input checked="" type="checkbox"/> BG Bulgaria | <input checked="" type="checkbox"/> MN Mongolia |
| <input checked="" type="checkbox"/> BR Brazil | <input checked="" type="checkbox"/> MW Malawi |
| <input checked="" type="checkbox"/> BY Belarus | <input checked="" type="checkbox"/> MX Mexico |
| <input checked="" type="checkbox"/> CA Canada | <input checked="" type="checkbox"/> NO Norway |
| <input checked="" type="checkbox"/> CH AND LI Switzerland and Liechtenstein | <input checked="" type="checkbox"/> NZ New Zealand |
| <input checked="" type="checkbox"/> CN China | <input checked="" type="checkbox"/> PL Poland |
| <input checked="" type="checkbox"/> CU Cuba | <input checked="" type="checkbox"/> PT Portugal |
| <input checked="" type="checkbox"/> CZ Czech Republic | <input checked="" type="checkbox"/> RO Romania |
| <input checked="" type="checkbox"/> DE Germany | <input checked="" type="checkbox"/> RU Russian Federation |
| <input checked="" type="checkbox"/> DK Denmark | <input checked="" type="checkbox"/> SD Sudan |
| <input checked="" type="checkbox"/> EE Estonia | <input checked="" type="checkbox"/> SE Sweden |
| <input checked="" type="checkbox"/> ES Spain | <input checked="" type="checkbox"/> SG Singapore |
| <input checked="" type="checkbox"/> FI Finland | <input checked="" type="checkbox"/> SI Slovenia |
| <input checked="" type="checkbox"/> GB United Kingdom | <input checked="" type="checkbox"/> SK Slovakia |
| <input checked="" type="checkbox"/> GE Georgia | <input checked="" type="checkbox"/> SL Sierra Leone |
| <input checked="" type="checkbox"/> GH Ghana | <input checked="" type="checkbox"/> TJ Tajikistan |
| <input checked="" type="checkbox"/> GM Gambia | <input checked="" type="checkbox"/> TM Turkmenistan |
| <input checked="" type="checkbox"/> GW Guinea-Bissau ▲▲ | <input checked="" type="checkbox"/> TR Turkey |
| <input checked="" type="checkbox"/> HU Hungary | <input checked="" type="checkbox"/> TT Trinidad and Tobago |
| <input checked="" type="checkbox"/> ID Indonesia | <input checked="" type="checkbox"/> UA Ukraine |
| <input checked="" type="checkbox"/> IL Israel | <input checked="" type="checkbox"/> UG Uganda |
| <input checked="" type="checkbox"/> IS Iceland | <input checked="" type="checkbox"/> US United States of America |
| <input checked="" type="checkbox"/> JP Japan | |
| <input checked="" type="checkbox"/> KE Kenya | <input checked="" type="checkbox"/> UZ Uzbekistan |
| <input checked="" type="checkbox"/> KG Kyrgyzstan | <input checked="" type="checkbox"/> VN Viet Nam |
| <input checked="" type="checkbox"/> KP Democratic People's Republic of Korea | <input checked="" type="checkbox"/> YU Yugoslavia |
| | <input checked="" type="checkbox"/> ZW Zimbabwe |
| <input checked="" type="checkbox"/> KR Republic of Korea | |
| <input checked="" type="checkbox"/> KZ Kazakstan | |
| <input checked="" type="checkbox"/> LC Saint Lucia | |
| <input checked="" type="checkbox"/> LK Sri Lanka | |
| <input checked="" type="checkbox"/> LR Liberia | |
| <input checked="" type="checkbox"/> LS Lesotho | |

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after the issuance of this sheet:

- ☒ HR Croatia
☒ GD Grenada
☒ IN India

In addition to the designations made above, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except the designation(s) of

The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

Supplemental Box *If the Supplemental Box is not used, this sheet should not be included in the request.*

1. *If, in any of the Boxes, the space is insufficient to furnish all the information: in such case, write "Continuation of Box No. ..." [indicate the number of the Box] and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient, in particular:*
 - (i) *if more than two persons are involved as applicants and/or inventors and no "continuation sheet" is available: in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below;*
 - (ii) *if, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant;*
 - (iii) *if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;*
 - (iv) *if, in addition to the agent(s) indicated in Box No. IV, there are further agents: in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;*
 - (v) *if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V, the name of the United States of America is accompanied by an indication "continuation" or "continuation-in-part": in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;*
 - (vi) *if, in Box No. VI, there are more than three earlier applications whose priority is claimed: in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI;*
 - (vii) *if, in Box No. VI, the earlier application is an ARIPO application: in such case, write "Continuation of Box No. VI", specify the number of the item corresponding to that earlier application and indicate at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed.*
2. *If, with regard to the precautionary designation statement contained in Box No. V, the applicant wishes to exclude any State(s) from the scope of that statement: in such case, write "Designation(s) excluded from precautionary designation statement" and indicate the name or two-letter code of each State so excluded.*
3. *If the applicant claims, in respect of any designated Office, the benefits of provisions of the national law concerning non-prejudicial disclosures or exceptions to lack of novelty: in such case, write "Statement concerning non-prejudicial disclosures or exceptions to lack of novelty" and furnish that statement below.*

PURVIS, William Michael Cameron
 COTTER, Ivan John
 PILCH, Adam John Michael
 CRISP, David Norman
 ROBINSON, Nigel Alexander Julian
 HARRIS, Ian Richard
 HARDING, Charles Thomas
 TURNER, James Arthur
 MALLALIEU, Catherine Louise
 PRATT, Richard Wilson
 PRICE, Paul Anthony King
 HOLMES, Miles
 HORNER, David Richard
 MASCHIO, Antonio
 NACHSHEN, Neil
 POTTER, Julian

Box No. VI PRIORITY CLAIMFurther priority claims are indicated in the Supplemental Box ☐

The priority of the following earlier application(s) is hereby claimed:

	Country (in which, or for which, the application was filed)	Filing Date (day/month/year)	Application No.	Office of filing (only for regional or international application)
item (1)	United Kingdom	09 Jan 1998 (09.01.98) ▲	9800487.2	
item (2)				
item (3)				

Mark the following check-box if the certified copy of the earlier application is to be issued by the Office which for the purposes of the present international application is the receiving Office (a fee may be required):

- ☒ The receiving Office is hereby requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s): (1)

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) (If two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):

ISA / EPO

Earlier Search Fill in where a search (international, international-type or other) by the International Search Authority has already been carried out or requested and the Authority is now requested to base the international search, to the extent possible, on the results of that earlier search. Identify such search or request either by reference to the relevant application (or the translation thereof) or by reference to the search request:

Country (or regional Office):

Date (day/month/year)

Number:

Box No. VII CHECK LIST

This international application contains the following number of sheets:

- | | | | | |
|----------------|---|-----------|---------------|---|
| 1. request | : | 5 | sheets | ✓ |
| 2. description | : | 35 | sheets | ✓ |
| 3. claims | : | 4 | sheets | ✓ |
| 4. abstract | : | 1 | sheets | ✓ |
| 5. drawings | : | 0 | sheets | |
| Total | : | 45 | sheets | ✓ |

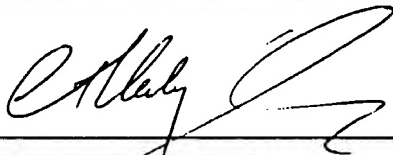
This international application is accompanied by the item(s) marked below:

- | | |
|--|--|
| 1. <input type="checkbox"/> separate signed power of attorney | 5. <input checked="" type="checkbox"/> fee calculation sheet ✓ |
| 2. <input type="checkbox"/> copy of general power of attorney | 6. <input type="checkbox"/> separate indications concerning deposited microorganisms |
| 3. <input type="checkbox"/> statement explaining lack of signature | 7. <input type="checkbox"/> nucleotide and/or amino acid sequence listing (diskette) |
| 4. <input type="checkbox"/> priority documents(s) identified in Box No. VI as item(s): | 8. <input checked="" type="checkbox"/> other (specify): Letter ✓ |

Figure No. _____ of the drawings (if any) should accompany the abstract when it is published

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request)



For receiving Office use only

1. Date of actual receipt of the purported international application:

08-01-99 08 JANUARY 1999

2. Drawings:

3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:

received:

4. Date of timely receipt of the required corrections under PCT Article 11(2):

not received:

5. International Searching Authority specified by the applicant:

ISA /

6.

Transmittal of search copy delayed until search fee paid

Date of receipt of the record copy by the International Bureau:

For International Bureau use only

The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent, with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line below:

IPEA/ EPO

PCT

DEMAND

CHAPTER II

under Article 31 of the Patent Cooperation Treaty:
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated).

For International Preliminary Examining Authority use only		
Identification of IPEA		Date of receipt of DEMAND
Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION		Applicant's or agent's file reference P005439WO CTH
International application No. PCT/GB99/00070	International filing date (day/month/year) 8 Jan 1999	(Earliest) Priority date (day/month/year) 9 Jan 1998
Title of invention MEDICAMENT		
Box No. II APPLICANT(S)		
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) OraTol Limited The Old Blue School Lower Square Isleworth Middlesex TW7 6RL United Kingdom		Telephone No.: Facsimile No.: Teleprinter No.:
State (that is, country) of nationality: GB		State (that is, country) of residence: GB
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) WILLIAMS, Neil Andrew 16 The Court Old Coach Road Cross, Axbridge Somerset, BS26 2EF United Kingdom		
State (that is, country) of nationality: GB		State (that is, country) of residence: GB
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) HIRST, Timothy Raymond 30 Albert Road Clevedon North Somerset BS21 7RR United Kingdom		
State (that is, country) of nationality: GB		State (that is, country) of residence: GB
<input checked="" type="checkbox"/> Further applicants are indicated on a continuation sheet.		

Continuation of Box No. II APPLICANT(S)

If none of the following sub-boxes is used, this sheet is not to be included in the demand.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

BIENENSTOCK, John
436 Wellington Street West
Toronto
Ontario
Canada
M5V 1E3

State (that is, country) of nationality: GB

State (that is, country) of residence: CA

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

State (that is, country) of nationality:

State (that is, country) of residence:

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

State (that is, country) of nationality:

State (that is, country) of residence:

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

State (that is, country) of nationality:

State (that is, country) of residence:

☐ Further applicants are indicated on another continuation sheet.

Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCEThe following person is ☒ agent ☐ common representativeand ☒ has been appointed earlier and represents the applicant(s) also for international preliminary examination.☐ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.Name and address: (Family name followed by given name; for a legal entity, full official designation.
The address must include postal code and name of country)HARDING, Charles Thomas
D Young & Co
21 New Fetter Lane
London
EC4A 1DA
United Kingdom

Telephone No.:

023 8063 4816

Facsimile No.:

023 8022 4262

Teleprinter No.:

477667 YOUNGS G

☐ Address for Correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.**Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION**

Statement concerning amendments: *

1. The applicant wishes the international preliminary examination to start on the basis of:

☒ the international application as originally filed

the description

☒ as originally filed☐ as amended under Article 34

the claims

☒ as originally filed☐ as amended under Article 19 (together with any accompanying statement)☐ as amended under Article 34

the drawings

☒ as originally filed☐ as amended under Article 342. ☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.3. ☐ The applicant wishes the start of the international preliminary examination to be postponed until the expiration of 20 months from the priority date unless the International Preliminary Examining Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). (This check-box may be marked only where the time limit under Article 19 has not yet expired).

* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: English

☒ which is the language in which the international application was filed.☐ which is the language of a translation furnished for the purposes of international search.☐ which is the language of publication of the international application.☐ which is the language of translation (to be) furnished for the purposes of international preliminary examination.**Box No. V ELECTION OF STATES**

The applicant hereby elects all eligible States (that is, all States which have been designated and which are bound by Chapter II of the PCT)

excluding the following States which the applicant wishes not to elect:

Box No. VI CHECK LIST

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:

- | | | | |
|----|---|---|--------|
| 1. | translation of international application | : | sheets |
| 2. | amendments under Article 34 | : | sheets |
| 3. | copy (or, where required, translation) of amendments under Article 19 | : | sheets |
| 4. | copy (or, where required, translation) of statement under Article 19 | : | sheets |
| 5. | letter | : | sheets |
| 6. | other (specify) | : | sheets |

For International Preliminary Examining Authority use only

- | received | not received |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |

The demand is also accompanied by the item(s) marked below:

- | | |
|--|---|
| 1. <input checked="" type="checkbox"/> fee calculation sheet | 4. <input type="checkbox"/> statement explaining lack of signature |
| 2. <input type="checkbox"/> separate signed power of attorney | 5. <input type="checkbox"/> nucleotide and or amino acid sequence listing in computer readable form |
| 3. <input type="checkbox"/> copy of general power of attorney; reference number, if any: | 6. <input checked="" type="checkbox"/> other (specify): Letter |

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).

MASCHIO, Antonio

For International Preliminary Examining Authority use only

- Date of actual receipt of DEMAND:
- Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):
- ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply.
 ☐ The applicant has been informed accordingly.
- ☐ The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5.
- ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.

For International Bureau use only

Demand received from IPEA on:

PCT

FEE CALCULATION SHEET

Annex to the Demand for international preliminary examination

International application No. PCT/GB99/00070	For International Preliminary Examining Authority use only
Applicant's or agent's file reference P005439WO CTH	Date stamp of the IPEA
Applicant <div style="text-align: center; margin-top: 10px;">ORATOL LIMITED</div>	
Calculation of prescribed fees	
1. Preliminary examination fee	EUR 1,533 P
2. Handling fee (<i>Applicants from certain states are entitled to a reduction of 75% of the handling fee. Where the applicant is (or all applicants are) so entitled, the amount to be entered at H is 25% of the handling fee.</i>)	EUR 148 H
3. Total of prescribed fees Add the amounts entered at P and H and enter total in the TOTAL box	<div style="border: 1px solid black; padding: 2px; margin-bottom: 2px;">EUR 1,681</div> <div style="border: 1px solid black; padding: 2px;">TOTAL</div>
Mode of Payment	
<input checked="" type="checkbox"/> authorization to charge deposit account with the IPEA (see below)	<input type="checkbox"/> cash
<input type="checkbox"/> cheque	<input type="checkbox"/> revenue stamps
<input type="checkbox"/> postal money order	<input type="checkbox"/> coupons
<input type="checkbox"/> bank draft	<input type="checkbox"/> other (<i>specify</i>):
Deposit Account Authorization (<i>this mode of payment may not be available at all IPEAs</i>)	
The IPEA/ <u>EPO</u> <input checked="" type="checkbox"/> is hereby authorized to charge the total fees indicated above to my deposit account.	
<input checked="" type="checkbox"/> (<i>this check-box may be marked only if the conditions for deposit accounts of the IPEA so permit</i>) is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.	
Deposit Account Number 28050042	Date (day/month/year) 3 Aug 1999
Signature Antonio Maschio	

PCT

FEE CALCULATION SHEET

Annex to the Demand for international preliminary examination

International application No. PCT/GB99/00070 <hr/> Applicant's or agent's file reference P005439WO CTH	For International Preliminary Examining Authority use only <hr/> Date stamp of the IPEA
Applicant <div style="text-align: center; margin-top: 10px;">ORATOL LIMITED</div>	
Calculation of prescribed fees <div style="display: flex; justify-content: space-between; align-items: flex-end;"> <div style="width: 60%;"> 1. Preliminary examination fee </div> <div style="width: 20%; text-align: center;">EUR 1,533</div> <div style="width: 10%; text-align: center; border: 1px solid black; padding: 2px;">P</div> </div> <div style="display: flex; justify-content: space-between; align-items: flex-end; margin-top: 20px;"> <div style="width: 60%;"> 2. Handling fee (<i>Applicants from certain states are entitled to a reduction of 75% of the handling fee. Where the applicant is (or all applicants are) so entitled, the amount to be entered at H is 25% of the handling fee.</i>) </div> <div style="width: 20%; text-align: center;">EUR 148</div> <div style="width: 10%; text-align: center; border: 1px solid black; padding: 2px;">H</div> </div> <div style="display: flex; justify-content: space-between; align-items: flex-end; margin-top: 20px;"> <div style="width: 60%;"> 3. Total of prescribed fees Add the amounts entered at P and H and enter total in the TOTAL box </div> <div style="width: 20%; text-align: center;">EUR 1,681</div> <div style="width: 10%;"></div> </div> <div style="display: flex; justify-content: space-between; align-items: flex-end; margin-top: 5px;"> <div style="width: 60%;"></div> <div style="width: 20%; text-align: center; border: 1px solid black; padding: 2px;">TOTAL</div> <div style="width: 10%;"></div> </div>	
Mode of Payment <div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <input checked="" type="checkbox"/> authorization to charge deposit account with the IPEA (see below) </div> <div style="width: 45%;"> <input type="checkbox"/> cash </div> </div> <div style="display: flex; justify-content: space-between; margin-top: 10px;"> <div style="width: 45%;"> <input type="checkbox"/> cheque </div> <div style="width: 45%;"> <input type="checkbox"/> revenue stamps </div> </div> <div style="display: flex; justify-content: space-between; margin-top: 10px;"> <div style="width: 45%;"> <input type="checkbox"/> postal money order </div> <div style="width: 45%;"> <input type="checkbox"/> coupons </div> </div> <div style="display: flex; justify-content: space-between; margin-top: 10px;"> <div style="width: 45%;"> <input type="checkbox"/> bank draft </div> <div style="width: 45%;"> <input type="checkbox"/> other (specify): </div> </div>	
Deposit Account Authorization (<i>this mode of payment may not be available at all IPEAs</i>) The IPEA/ <u>EPO</u> <input checked="" type="checkbox"/> is hereby authorized to charge the total fees indicated above to my deposit account. <div style="text-align: center; margin-top: 10px;"> <input checked="" type="checkbox"/> (<i>this check-box may be marked only if the conditions for deposit accounts of the IPEA so permit</i>) is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account. </div> <div style="display: flex; justify-content: space-between; margin-top: 20px;"> <div style="width: 30%;"> 28050042 Deposit Account Number </div> <div style="width: 30%;"> 3 Aug 1999 Date (day/month/year) </div> <div style="width: 30%;"> Signature <div style="text-align: right; margin-top: 5px;">Antonio Maschio</div> </div> </div>	

PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

HARDING, Charles Thomas
D YOUNG & CO
21 New Fetter Lane
London EC4A 1DA
GRANDE BRETAGNE

SOUTHAMPTON

NOV 1999

PCT

WRITTEN OPINION

(PCT Rule 66)

Date of mailing
(day/month/year)

4. 11. 99

Applicant's or agent's file reference

P5439WO CTH

REPLY DUE

within 3 month(s)

from the above date of mailing

International application No.

PCT/GB99/00070

International filing date (day/month/year)

08/01/1999

Priority date (day/month/year)

09/01/1998

International Patent Classification (IPC) or both national classification and IPC

A61K38/16

Applicant

ORATOL LIMITED et al.

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.
2. This opinion contains indications relating to the following items:
 - I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain document cited
 - VII ☐ Certain defects in the international application
 - VIII ☒ Certain observations on the international application
3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.
4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 09/05/2000.

Name and mailing address of the international preliminary examining authority:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer / Examiner

Thalmair, M

Formalities officer (incl. extension of time limits)

THORNTON, J

Telephone No. +49 89 2399 8072



WRITTEN OPINION

International application No. PCT/GB99/00070

I. Basis of the opinion

1. This opinion has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".*):

Description, pages:

1-35 as originally filed

Claims, No.:

1-19 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 4-10, 12-15, 18,

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 4-10, 12-15, 18 are so unclear that no meaningful opinion could be formed (*specify*):

WRITTEN OPINION

International application No. PCT/GB99/00070

see separate sheet

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-3,11,16,17,19 (no)
Inventive step (IS)	Claims	1-3,11,16,17,19 (no)
Industrial applicability (IA)	Claims	1-19 (yes)

2. Citations and explanations

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Section III and VIII

The subject-matter of claim 4 referring to an assay method for identifying an agent according to any one of preceding claims 1 to 3 is so unclear (Art. 6 PCT) that no meaningful opinion with respect to novelty and inventive step could be established. In particular the phrasing "modulation of the ganglioside associated activity such that it is indicative that the agent may be capable of affecting an allergic condition and/or a hypersensitivity condition" does not enable the skilled person to know without undue experimentation which modulation is actually meant, i.e. capable of affecting an allergic and/or hypersensitivity condition. Thus, a determination of an agent seems to be impossible with regard to the claimed steps, since necessary technical features characterizing the assay method in a clear and precise manner are missing (but are comprised for instance in the description on page 33, line 6 to page 34, line 15). This refers also to subsequent claims 5-10, 12-15, 18 which are related directly or indirectly to claim 4.

Additionally the subject-matter of claims 1-3 seems to be unclear (Art. 6 PCT) with respect to the agent, which is characterized mainly by functional means. It remains doubtful in particular, which kind of modulation of the ganglioside associated activity is capable of affecting an allergic / hypersensitivity condition.

Moreover, the subject-matter of claim 12 is completely unclear (Art. 6 PCT), since no technical feature is provided which characterizes the claimed agent. The modulation of a ganglioside associated activity is considered as mere discovery of the mode of action.

Furthermore, claim 19 relies in respect of the technical features of the invention on references to the description contravening Rule 6.2 (a) PCT.

Section V

The subject-matter of claims 1-3 does not appear to be novel in view of the documents D 6 (WO-A-9112818) and D 7 (US-P-5 614 611), which are not cited in the International search report. Copies of these documents are appended hereto.

D 6 already shows the use of Staphylococcal enterotoxin to reduce immune

**WRITTEN OPINION
SEPARATE SHEET**

International application No. PCT/GB99/00070

responsiveness and especially to treat allergic responses, rhinitis, asthma (see page 5, lines 12-14; page 2, last paragraph to page 3, first two lines of D 6; c.f. page 20, lower part of the description of the present application).

Additionally, D 7 already discloses an agent which seems to fulfill the requirements as claimed in claims 1-3, namely monoclonal antibodies specific for membrane bound IgE on B cells which can be used alone to treat IgE-mediated allergy (such as extrinsic bronchial asthma, allergic rhinitis, food and drug allergies, see column 2, last paragraph of D 7).

However, even if novelty can be established for instance by disclaiming the agents used in D 6 and D 7, the subject-matter of claims 1-3 does not seem to involve inventive merits (Art. 33 (1,3) PCT) in view of D 1 (Nashar et al., 1997) and D 2 (Nashar et al., 1996).

These documents show that the B subunit of E. coli heat-labile enterotoxin (EtxB) exerts profound effects on immune cells via direct GM1-mediated immunomodulation of lymphocytes (see summary and abstract, respectively).

Although allergic or hypersensitivity conditions are not mentioned explicitly in D 1 / D 2, the person skilled in immunology would have got an incentive from the teachings of these documents to use EtxB in allergy which is a hypersensitive state acquired through exposure to a particular allergen and characterized by a diseased immune responsiveness.

The subject-matter of claim 11 does not seem to be novel (Art. 33 (1,2) PCT), since the agent EtxB is already known as potent mucosal and systemic immunogen (see D 1 and D 2) regardless of the process of identifying this agent.

Consequently, also the subject-matter of claims 16 and 17 is not novel (as they refer back to claim 11).

Furthermore, the subject-matter of claim 19 does not appear to be novel, since for instance E. coli heat labile enterotoxin (Etx) and its closely related homologue cholera toxin (Ctx) described in the description (page 3, last paragraph) are already known agents that bind and cross-link a ubiquitous cell glycolipid receptor, namely ganglioside GM1, and are recognized as potent mucosal and systemic immunogens (see D 1, summary, first lines).



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D-80298 München
☎ +49 89 2399-0
TX 523 656 epmu d
FAX +49 89 2399-4465

**Europäisches
Patentamt**

Generaldirektion 2

**European
Patent Office**

Directorate General 2

**Office européen
des brevets**

Direction Générale 2

Correspondence with the EPO on PCT Chapter II demands

In order to ensure that your PCT Chapter II demand is dealt with as promptly as possible you are requested to use the enclosed self-adhesive labels with any correspondence relating to the demand sent to the Munich Office.

One of these labels should be affixed to a prominent place in the upper part of the letter or form etc. which you are filing.

PATENT COOPERATION TREATY

PCT

09/600060

REC'D 07 APR 2000

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P5439WO CTH	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB99/00070	International filing date (day/month/year) 08/01/1999	Priority date (day/month/year) 09/01/1998
International Patent Classification (IPC) or national classification and IPC A61K38/16		
Applicant ORATOL LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


2. This REPORT consists of a total of 5 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 03/08/1999	Date of completion of this report 05.04.2000
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Thalmair, M Telephone No. +49 89 2399 2177



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/00070

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-35 as originally filed

Claims, No.:

1-19 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
☒ claims Nos. 4-10,12-15,18 (for novelty and inventive step).

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/00070

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 4-10,12-15,18 are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1-3,11,16,17,19
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-3,11,16,17,19
Industrial applicability (IA)	Yes:	Claims	1-19
	No:	Claims	

2. Citations and explanations

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/00070

Section III and Section VIII

The subject-matter of claim 4 referring to an assay method for identifying an agent according to any one of preceding claims 1 to 3 is so unclear (Art. 6 PCT) that no meaningful opinion with respect to novelty and inventive step could be established. In particular the phrasing "modulation of the ganglioside associated activity such that it is indicative that the agent may be capable of affecting an allergic condition and/or a hypersensitivity condition" does not enable the skilled person to know without undue experimentation which modulation is actually meant, i.e. capable of affecting an allergic and/or hypersensitivity condition. Thus, a determination of an agent seems to be impossible with regard to the claimed steps, since necessary technical features characterizing the assay method in a clear and precise manner are missing (but are comprised for instance in the description on page 33, line 6 to page 34, line 15). This refers also to subsequent claims 5-10, 12-15, 18 which are related directly or indirectly to claim 4.

Additionally the subject-matter of claims 1-3 seems to be unclear (Art. 6 PCT) with respect to the agent, which is characterized mainly by functional means. It remains doubtful in particular, which kind of modulation of the ganglioside associated activity is capable of affecting an allergic / hypersensitivity condition.

Moreover, the subject-matter of claim 12 is completely unclear (Art. 6 PCT), since no technical feature is provided which characterizes the claimed agent. The modulation of a ganglioside associated activity is considered as mere discovery of the mode of action.

Furthermore, claim 19 relies in respect of the technical features of the invention on references to the description contravening Rule 6.2 (a) PCT.

Section V

The subject-matter of claims 1-3 does not appear to be novel in view of the documents D 6 (WO-A-9112818) and D 7 (US-P-5614611), which are not cited in the International Search Report (see Guidelines C-VI, 8.9).
D 6 already shows the use of Staphylococcal enterotoxin to reduce immune

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/00070

responsiveness and especially to treat allergic responses, rhinitis, asthma (see page 5, lines 12-14; page 2, last paragraph to page 3, first two lines of D 6; c.f. page 20, lower part of the description of the present application).

Additionally, D 7 already discloses an agent which seems to fulfill the requirements as claimed in claims 1-3, namely monoclonal antibodies specific for membrane bound IgE on B cells which can be used alone to treat IgE-mediated allergy (such as extrinsic bronchial asthma, allergic rhinitis, food and drug allergies, see column 2, last paragraph of D 7).

However, even if novelty can be established for instance by disclaiming the agents used in D 6 and D 7, the subject-matter of claims 1-3 does not seem to involve inventive merits (Art. 33 (1,3) PCT) in view of D 1 (Nashar et al., 1997) and D 2 (Nashar et al., 1996).

These documents show that the B subunit of E. coli heat-labile enterotoxin (EtxB) exerts profound effects on immune cells via direct GM1-mediated immunomodulation of lymphocytes (see summary and abstract, respectively).

Although allergic or hypersensitivity conditions are not mentioned explicitly in D 1 / D 2, the person skilled in immunology would have got an incentive from the teachings of these documents to use EtxB in allergy which is a hypersensitive state acquired through exposure to a particular allergen and characterized by a diseased immune responsiveness.

The subject-matter of claim 11 does not seem to be novel (Art. 33 (1,2) PCT), since the agent EtxB is already known as potent mucosal and systemic immunogen (see D 1 and D 2) regardless of the process of identifying this agent.

Consequently, also the subject-matter of claims 16 and 17 is not novel (as they refer back to claim 11).

Furthermore, the subject-matter of claim 19 does not appear to be novel, since for instance E. coli heat labile enterotoxin (Etx) and its closely related homologue cholera toxin (Ctx) described in the description (page 3, last paragraph) are already known agents that bind and cross-link a ubiquitous cell glycolipid receptor, namely ganglioside GM1, and are recognized as potent mucosal and systemic immunogens (see D 1, summary, first lines).

PATENT COOPERATION TREATY

SOUTHAMPTON

7 JUN 1999

DSC TH

PCT

From the INTERNATIONAL SEARCHING AUTHORITY

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

To:
D. YOUNG & CO.
Attn. HARDING, C.
21 New Fetter Lane
London EC4A 1DA
UNITED KINGDOM

Date of mailing
(day/month/year) 01/06/1999

Applicant's or agent's file reference
P5439WO CTH

FOR FURTHER ACTION See paragraphs 1 and 4 below

International application No.
PCT/GB 99/00070

International filing date
(day/month/year) 08/01/1999

Applicant

ORATOL LIMITED et al.

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Claudia Aragone

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference P5439W0 CTH	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 99/ 00070	International filing date (day/month/year) 08/01/1999	(Earliest) Priority Date (day/month/year) 09/01/1998
Applicant ORATOL LIMITED et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

AGENT FOR TREATING ALLERGIC OR HYPERSENSITIVITY CONDITION

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB 99/ 00070

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 9-12, 16, 17
because they relate to subject matter not required to be searched by this Authority, namely:
See FURTHER INFORMATION SHEET PCT/ISA/210
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Although claim 14 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Claims Nos.: 9-12, 16,17

Claims 9-12, 16 and 17 respectively relating to a agent identified by the process of claims 6-8 and a pharmaceutical composition containing the identified agent could not be searched completely as their subject matter were not sufficiently disclosed.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/00070

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61K38/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NASHAR T O ET AL: "Modulation of B-cell activation by the B subunit of Escherichia coli enterotoxin: receptor interaction up-regulates MHC class II, B7, CD40, CD25 and ICAM-1." IMMUNOLOGY, (1997 AUG) 91 (4) 572-8, XP002102696 see the whole document ---	1,2,4, 14,15, 17-19
A	NASHAR T O ET AL: "POTENT IMMUNOGENICITY OF THE B SUBUNITS OF ESCHERICHIA COLI HEAT-LABILE ENTEROTOXIN: RECEPTOR BINDING IS ESSENTIAL AND INDUCES DIFFERENTIAL MODULATION OF LYMPHOCYTE SUBSETS" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 93, no. 1, 1 January 1996, pages 226-230, XP002019422 --- -/--	1-19

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"G" document member of the same patent family

Date of the actual completion of the international search

14 May 1999

Date of mailing of the international search report

01/06/1999

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/00070

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	YANKELEVICH B ET AL: "PREVENTION OF ACUTE GRAFT-VERSUS-HOST DISEASE BY TREATMENT WITH A NOVEL IMMUNOSUPPRESSANT. CHOLERA TOXIN B SUBUNIT" JOURNAL OF IMMUNOLOGY, vol. 154, no. 7, 1 January 1995, pages 3611-3617, XP002019424 -----	1-19
A	WO 97 02045 A (UNIVERSITY OF BRISTOL) 23 January 1997 cited in the application see the whole document -----	1-19
A	WO 95 10301 A (HOLMGREN K ET AL.) 20 April 1995 cited in the application see the whole document -----	1-19

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/00070

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9702045 A	23-01-1997	AU 6314296 A	05-02-1997
		CA 2225788 A	23-01-1997
		CN 1192693 A	09-09-1998
		CZ 9800012 A	17-06-1998
		EP 0841939 A	20-05-1998
		NO 980005 A	05-03-1998
		PL 324424 A	25-05-1998
WO 9510301 A	20-04-1995	US 5681571 A	28-10-1997
		AT 165515 T	15-05-1998
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		DE 69409962 D	04-06-1998
		DE 69409962 T	27-08-1998
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		SE 9303301 A	09-04-1997